

# **ODIN:**

## **OntoGene Document Inspector**

User Manual, v 0.5

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<http://www.ontogene.org/>

### **Introduction**

ODIN is a lightweight graphical interface for literature curation that can be run within a web browser.

Currently ODIN is coupled with the OntoGene pipeline which provides its text mining capabilities, however nothing prevents ODIN from being interfaced with other text mining services as long as they support the same data exchange format.

In order to achieve optimal performance and user satisfaction, the OntoGene team typically customizes the OntoGene pipeline and ODIN for the specific curation task. OntoGene and ODIN have already been customized for some experiments in assisted curation in collaboration with well known databases, in particular PharmGKB, CTD and RegulonDB, which have been described in a number of journal publications. For details please see: [www.ontogene.org](http://www.ontogene.org)

The purpose of this manual is to describe how ODIN can be used by a curator to perform some literature-based curation tasks, as for example exploring the entity annotations of a given article, or validate interactions suggested by the system.

For any problem, comment or suggestion please contact us at [odin@ontogene.org](mailto:odin@ontogene.org)

Best regards,  
The OntoGene Team  
<http://www.ontogene.org/>

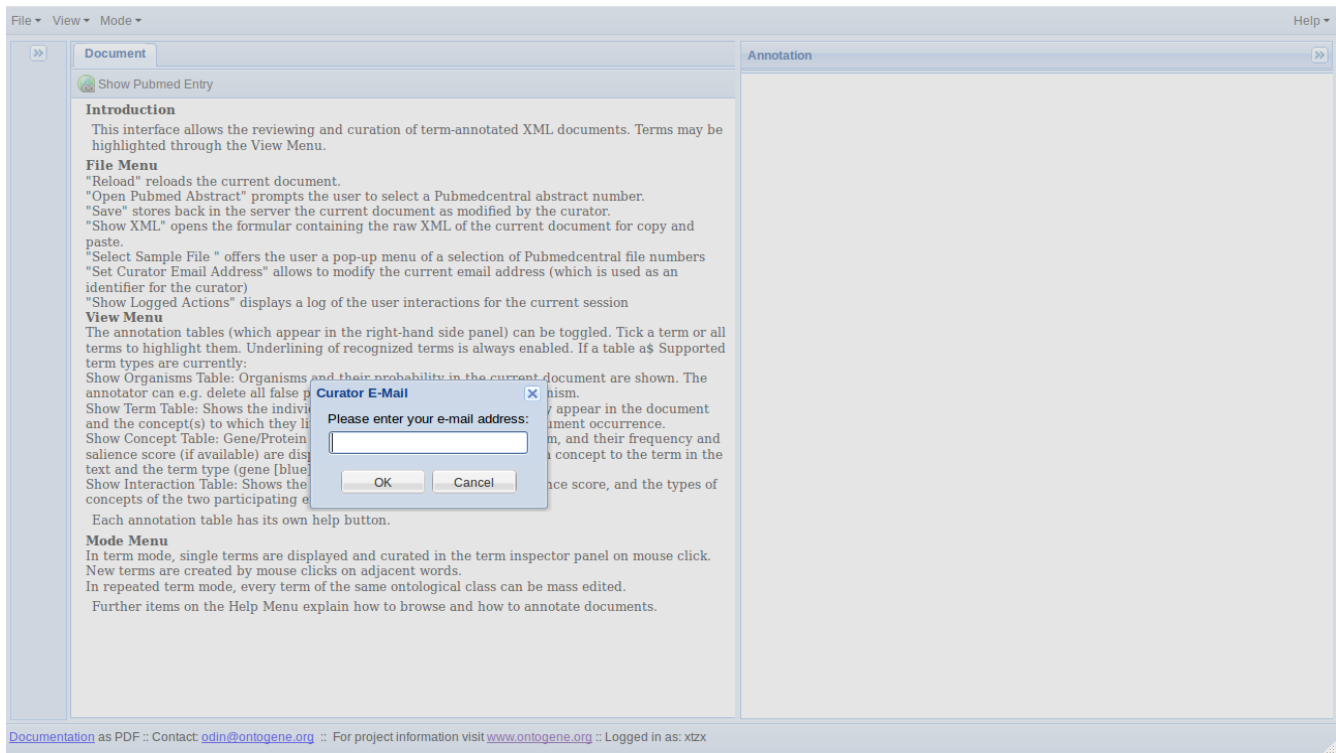
## 1. Getting Started

Enter your curator identifier in order to log in. At least 2 characters are required.

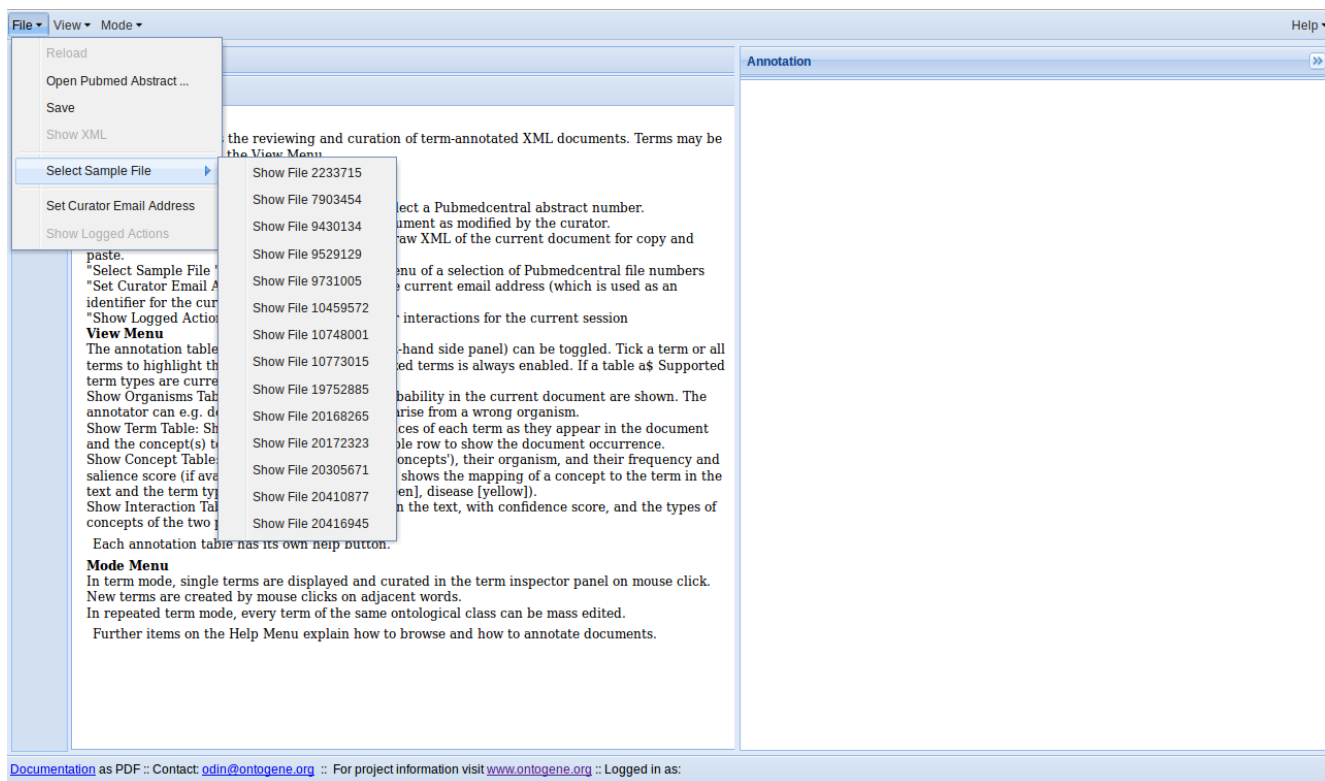
Only alphanumeric characters, and the symbols '@', '-' and '.' are allowed. It does not need to be an email address, but make sure it is unique and use it consistently.

If you reload the page later on, or open a new window, logging in by entering a curator identifier is not necessary anymore as your curator id will be saved in your browser as a cookie.

If you want to change the curator id at any moment in the future, this is possible by choosing *Set Curator Identifier* from the *File* menu.



Once you are logged into the system, select a file to inspect. You can either use *Open Pubmed Abstract* from the *File* menu or you can also select one of the provided sample files from *Select Sample File*, as shown below.



The *Open Pubmed Abstract* option allows you to enter any pubmed identifier. The OntoGene system will fetch the corresponding abstract from PubMed and process it, before delivering the results to the ODIN interface. The process could last a couple of seconds, depending on the length of the abstract.

## 2. The ODIN panels

Below you can see an example of an annotated document: the PubMed abstract is in the *Document* panel (left in the picture) and the interactions appear in the *Annotation* panel (right side of the picture). If the *Annotation* panel is empty, you can select an annotation type in the *View* menu. The available annotations depend on the version of ODIN and the customized application. Typically, they are application-specific concepts (such as genes, proteins, diseases, organisms), and interactions among them. In the example we see interaction annotation. The concepts annotation has also been selected in the *View*-menu, and can be brought to the foreground by clicking on the *Concepts*-tab in the *Annotation*-panel.

A brief online introduction to each annotation table is also available, in the *Help*-menu within the *Annotation*-panel (top right corner). [The *Help*-menu is currently being revised]

The screenshot displays the ODIN software interface. The main window is titled "Document PMID 2233715" and contains a PubMed abstract. The abstract text is as follows:

**On the mechanism for efficient repression of the interleukin-6 promoter by glucocorticoids : enhancer , TATA box , and RNA start site ( Inr motif ) occlusion .**

**Abstract** The feedback inhibition of [interleukin-6](#) ( [IL-6](#) ) gene expression by [glucocorticoids](#) , represents a regulatory link between the endocrine and immune systems . The mechanism of the efficient repression of the [IL-6](#) promoter by [dexamethasone](#) ( [Dex](#) ) was investigated in HeLa cells transiently transfected with plasmid constructs containing different [IL-6](#) promoter elements linked to the herpesvirus thymidine kinase gene ( [tk](#) ) promoter and the bacterial [chloramphenicol](#) acetyltransferase gene ( [cat](#) ) and cotransfected with cDNA vectors constitutively expressing either the active wild-type or inactive mutant human [glucocorticoid receptor](#) ( [GR](#) ) . The induction by [interleukin-1](#) , [tumor necrosis factor](#) , phorbol ester , or [forskolin](#) of [IL-6](#) - [tk](#) - [cat](#) chimeric constructs containing a single copy of the [IL-6](#) DNA segment from - 173 to - 151 ( MRE I ) or from - 158 to - 145 ( MRE II ) , which derive from within the multiple [cytokine](#) - and second-messenger-responsive enhancer ( MRE ) region , was strongly repressed by [Dex](#) in a wild-type [GR](#) - dependent fashion irrespective of the inducer used . The induction by [pseudorabies](#) virus of an [IL-6](#) construct containing the [IL-6](#) , [TATA box](#) , and the RNA start site ( " initiator " or Inr element ) but not the MRE region was also repressed by [Dex](#) in the presence of wild-type [GR](#) . DNase I footprinting showed that the purified [DNA-binding](#) fragment of [GR](#) bound across the MRE , the [TATA box](#) , and the Inr site in the [IL-6](#) promoter ; this footprint overlapped that produced by proteins present in nuclear extracts from uninduced or induced HeLa cells . Imperfect palindromic nucleotide sequence motifs moderately related to the consensus [GR](#) - responsive element ( GRE ) motif were present at the Inr , the [TATA box](#) , and the MRE II site in the [IL-6](#) promoter ; although MRE I and a [GR](#) - binding site between - 201 and - 210 in IL-6 both lacked a discernible inverted repeat motif , their sequences showed considerable similarity with negative GRE sequences in other [Dex](#) - repressed genes . Surprisingly , chimeric genes containing MRE II , which lacks a recognizable GACGTCA cyclic [AMP](#) - and phorbol ester-responsive motif , were strongly induced by both phorbol ester and [forskolin](#) , suggesting that MRE II ( ACATTGCACAACTCT ) may be the prototype of a novel cyclic [AMP](#) - and phorbol ester-responsive element . Taken together , these observations suggest that ligand-activated [GR](#) represses the [IL-6](#) gene by occlusion not only of the [inducible](#) [IL-6](#) MRE enhancer region but also of the basal [IL-6](#) promoter elements .

[Interleukin-1](#) ; [Interleukin-6](#) ; Oligonucleotide Probes ; RNA ; [Neoplasm](#) ; Receptors ; Glucocorticoid ; [Tumor Necrosis Factor-alpha](#) ; Tetradecanoylphorbol Acetate ; [Dexamethasone](#) ; [Forskolin](#) ; Base Sequence ; [Dexamethasone](#) ; pharmacology ; Enhancer Elements , Genetic ; drug effects ; Feedback ; [Forskolin](#) ; pharmacology ; Gene Expression ; drug effects ; Genes , Suppressor ; drug effects ; HeLa Cells ; drug effects ; immunology ; Humans ; [Interleukin-1](#) ; pharmacology ; [Interleukin-6](#) ; genetics ; Molecular Sequence Data ; Oligonucleotide Probes ; Promoter Regions , Genetic ; RNA ; [Neoplasm](#) ; drug effects ; genetics ; Receptors ; Glucocorticoid ; genetics ; metabolism ; Restriction Mapping ; Second Messenger Systems ; [TATA Box](#) ; drug effects ; Tetradecanoylphorbol Acetate ; pharmacology ; Transcription , Genetic ; Transfection ; [Tumor Necrosis Factor-alpha](#) ; pharmacology ;

The right panel, titled "Annotation", shows a table of interactions. The table has columns for "Conf", "Type", "Concept 1", "Name 1", "Type", "Concept 2", "Name 2", and "Help". The data rows are:

Conf	Type	Concept 1	Name 1	Type	Concept 2	Name 2	Help
1.00	Drug	PA452347	glucocorticoi	Gene	PA198	IL6	
0.99	Drug	PA449247	dexamethas	Gene	PA198	IL6	

At the bottom of the interface, there is a footer with the following text: "Documentation as PDF :: Contact: [odin@ontogene.org](mailto:odin@ontogene.org) :: For project information visit [www.ontogene.org](http://www.ontogene.org) :: Logged in as:

ODIN has actually 3 panels (see figure below): on the left the *Inspector* panel, in the center the *Document* panel, and on the right the *Annotations* panel. The *Inspector* panel is closed at the beginning and opens automatically if you click on a term, or if you click the double arrow on its top (at the left of the interface). In the same way, you can also open and close the *Annotation* panel on the right. We will discuss the *Inspector* panel in section 5.

The screenshot shows the ODIN (OntoGene.org) interface in Mozilla Firefox. The interface is divided into three main panels: Inspector (left), Document (center), and Annotations (right).

**Inspector Panel (Left):**

- Term Inspector:**
  - Term: dexamethasone
  - Term Type: DRUG
  - Concept Values: PA449247
  - Term Properties: Value: PA449247, Type: DRUG
  - Comment: (empty text area)
  - Search Databases:
    - Search Term Text: (input field)
    - ☒ PharmGKB
    - ☐ Entrez
    - ☐ UniProt

**Document Panel (Center):**

Document PMID 2233715

Show PubMed Entry

**On the mechanism for efficient repression of the interleukin-6 promoter by glucocorticoids : enhancer, TATA box, and RNA start site ( lnr motif ) occlusion .**

**Abstract** The feedback inhibition of interleukin-6 ( IL-6 ) gene expression by glucocorticoids represents a regulatory link between the endocrine and immune systems . The mechanism of the efficient repression of the IL-6 promoter by dexamethasone ( Dex ) was investigated in HeLa cells transiently transfected with plasmid constructs containing different IL-6 promoter elements ( tk ) promoter and the gene ( cat ) and cotransfected either the active wild-type or inactive mutant human glucocorticoid receptor ( GR ) . The induction by interleukin-1 , tumor necrosis factor , phorbol ester , or forskolin of IL-6 - tk - cat chimeric constructs containing a single copy of the IL-6 DNA segment from - 173 to - 151 ( MRE I ) or from - 158 to - 145 ( MRE II ) , which derive from within the multiple cytokine - and second-messenger-responsive enhancer ( MRE ) region , was strongly repressed by Dex in a wild-type GR - dependent fashion irrespective of the inducer used . The induction by pseudorabies virus of an IL-6 construct containing the IL-6 TATA box and the RNA start site ( " initiator " or lnr element ) but not the MRE region was also repressed by Dex in the presence of wild-type GR . DNase I footprinting showed that the purified DNA-binding fragment of GR bound across the MRE , the TATA box , and the lnr site in the IL-6 promoter ; this footprint overlapped that produced by proteins present in nuclear extracts from uninduced or induced HeLa cells . Imperfect palindromic nucleotide sequence motifs moderately related to the consensus GR - responsive element ( GRE ) motif were present at the lnr , the TATA box , and the MRE II site in the IL-6 promoter ; although MRE I and a GR - binding site between - 201 and - 210 in IL-6 both lacked a discernible inverted repeat motif , their sequences showed considerable similarity with negative GRE sequences in other Dex - repressed genes . Surprisingly , chimeric genes containing MRE II , which lacks a recognizable GACGTCA cyclic AMP - and phorbol ester-responsive motif , were strongly induced by both phorbol ester and forskolin , suggesting that MRE II ( ACATTGCACAATCT ) may be the prototype of a novel cyclic AMP - and phorbol ester-responsive element . Taken together , these observations suggest that ligand-activated GR represses the IL-6 gene by occlusion not only of the inducible

**Annotations Panel (Right):**

Annotations

Concepts Interactions

Reload Finish & Save Help

Conf	Type 1	Name 1	Type 2	Name 2				
<input checked="" type="checkbox"/>	Drug	dexamethasone	Gene	IL6	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	Drug	glucocorticoids	Gene	IL6	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Documentation as PDF :: Contact: [odin@ontogene.org](mailto:odin@ontogene.org) :: For project information visit [www.ontogene.org](http://www.ontogene.org) :: Logged in as:

It is also possible to visualize in a separate browser window the original PubMed entry from the PubMed webpage for the current article (click on *Show PubMed Entry* on top of the *Document* panel). Note that this functionality will not work correctly if your browser has a popup blocker.

The screenshot shows the OntoGene.org web application running in a Mozilla Firefox browser. The main content area displays the abstract of a PubMed article (PMID 2233715) titled "On the mechanism for efficient repression of the interleukin-6 promoter by glucocorticoids: enhancer, TATA box, and RNA start site (Inr motif) occlusion." The abstract text is visible, discussing the feedback inhibition of interleukin-6 gene expression by glucocorticoids. A "Show PubMed Entry" button is located at the top of the document panel. On the right, an "Annotation" panel shows a table of interactions between "dexamethasone" and "IL6". Below the main text, there are sections for "Related citations" and "Cited by 29 PubMed Central articles". The browser's address bar shows the URL "OntoGene.org: pharmgkb - Mozilla Firefox".

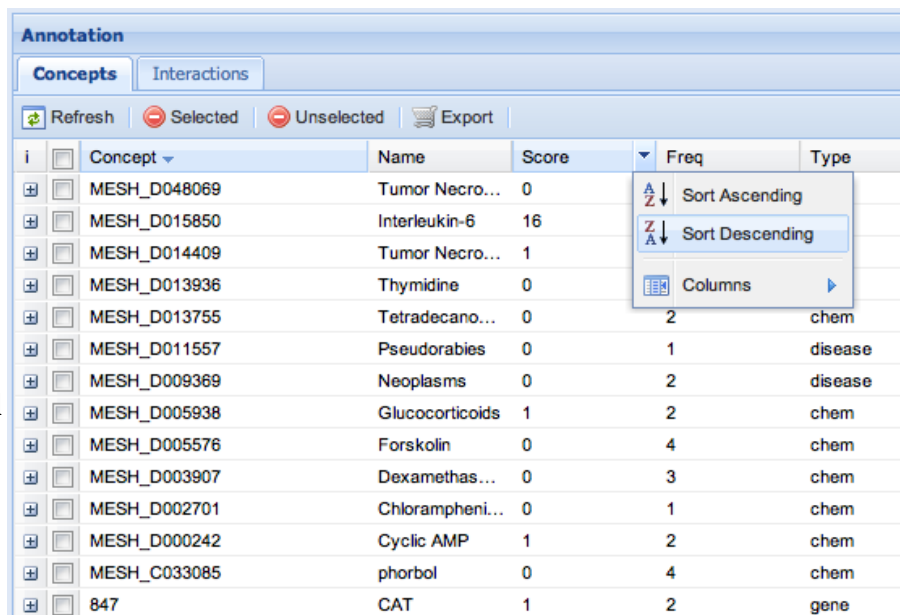
If you are unhappy about what you have done so far on an article, you can reload it using the *Reload* option from the *File* menu. Beware: all your actions so far on that article will be lost! We will show how to save your work in section 7.

### 3. Working with Concepts

Click on the *Concepts* tab in the *Annotation* panel. All concepts are displayed. Clicking on the right of the column title, you can sort them by the column of your choice.

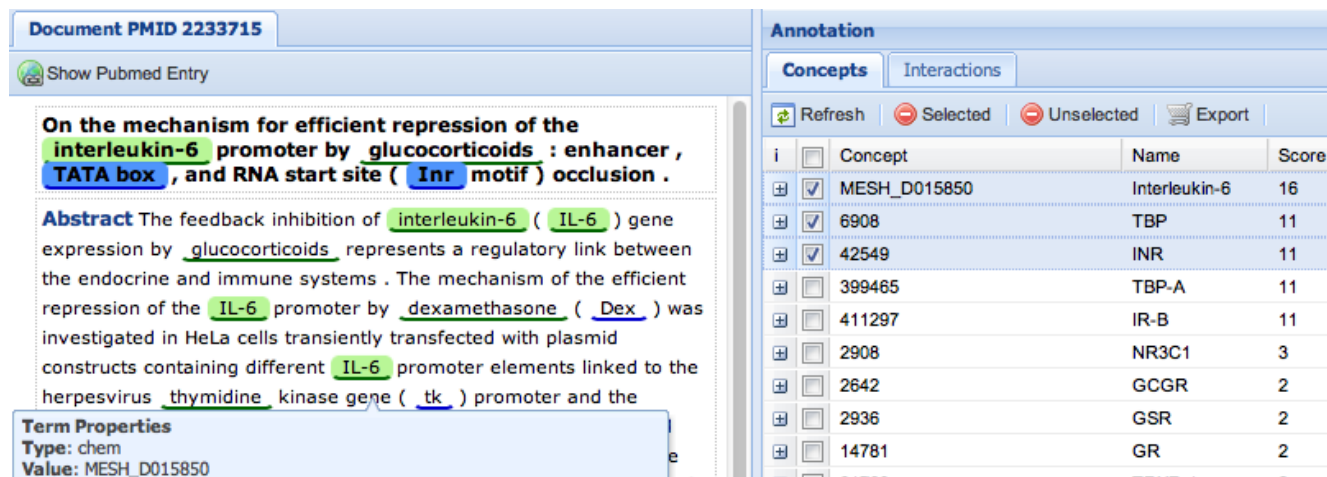
If you drag the column fringe, the column gets broader or smaller.

If you double-click on a concept or name, a definition is provided in a separate window. ODIN tries to provide this definition from a reference database. Which database is used for reference depends on the specific application for which ODIN has been customized.



i	Concept	Name	Score	Freq	Type
<input type="checkbox"/>	MESH_D048069	Tumor Necro...	0		
<input type="checkbox"/>	MESH_D015850	Interleukin-6	16		
<input type="checkbox"/>	MESH_D014409	Tumor Necro...	1		
<input type="checkbox"/>	MESH_D013936	Thymidine	0		
<input type="checkbox"/>	MESH_D013755	Tetradecano...	0	2	chem
<input type="checkbox"/>	MESH_D011557	Pseudorabies	0	1	disease
<input type="checkbox"/>	MESH_D009369	Neoplasms	0	2	disease
<input type="checkbox"/>	MESH_D005938	Glucocorticoids	1	2	chem
<input type="checkbox"/>	MESH_D005576	Forskolin	0	4	chem
<input type="checkbox"/>	MESH_D003907	Dexamethas...	0	3	chem
<input type="checkbox"/>	MESH_D002701	Chlorampheni...	0	1	chem
<input type="checkbox"/>	MESH_D000242	Cyclic AMP	1	2	chem
<input type="checkbox"/>	MESH_C033085	phorbol	0	4	chem
<input type="checkbox"/>	847	CAT	1	2	gene

Ticking the box on the left highlights all occurrences of the corresponding concept in the text.



**Document PMID 2233715**

Show Pubmed Entry

**On the mechanism for efficient repression of the interleukin-6 promoter by glucocorticoids : enhancer , TATA box , and RNA start site ( Inr motif ) occlusion .**

**Abstract** The feedback inhibition of interleukin-6 ( IL-6 ) gene expression by glucocorticoids represents a regulatory link between the endocrine and immune systems . The mechanism of the efficient repression of the IL-6 promoter by dexamethasone ( Dex ) was investigated in HeLa cells transiently transfected with plasmid constructs containing different IL-6 promoter elements linked to the herpesvirus thymidine kinase gene ( \_tk\_ ) promoter and the

**Term Properties**  
Type: chem  
Value: MESH\_D015850

**Annotation**

Concepts Interactions

Refresh Selected Unselected Export

i	Concept	Name	Score
<input checked="" type="checkbox"/>	MESH_D015850	Interleukin-6	16
<input checked="" type="checkbox"/>	6908	TBP	11
<input checked="" type="checkbox"/>	42549	INR	11
<input type="checkbox"/>	399465	TBP-A	11
<input type="checkbox"/>	411297	IR-B	11
<input type="checkbox"/>	2908	NR3C1	3
<input type="checkbox"/>	2642	GCGR	2
<input type="checkbox"/>	2936	GSR	2
<input type="checkbox"/>	14781	GR	2

You can delete all selected or unselected concept occurrences in the document using the red buttons on top of the *Annotation* panel.

You can mark all concepts of a certain type by selecting *Mark by concept type* from the *View* menu.

A search in the reference databases (which depend on the application) can be launched by double-clicking on a concept name or identifier, or by clicking on the plus-symbol at the beginning of a line.

## 4. Filtering options

You can use filtering options, which we describe now. Applying filters only displays the sentences of interest to the annotator.

- *Focus* filter: click on *Focus* in the *Concepts* tab (*Annotation* panel) to only display sentences that contain highlighted concepts according to your selection. The following example shows a view of a document in which the three most frequent terms were selected for highlighting, before and after clicking on *Focus*.

**Document PMID 12029051**

Show Pubmed Entry

S1 JOURNAL OF BACTERIOLOGY , June 2002 , p .  
S2 3338 - 3347 Vol .  
S3 184 , No . 12 .  
S4 Copyright © 2002 , American Society for Microbiology .  
S5 All Rights Reserved .  
S6 Dam - and OxyR - Dependent Phase Variation of agn43 : Essential Elements and Evidence for a New Role of DNA Methylation .  
S7 Anu Wallecha , Vincent Munster , Jason Correnti , Teresa Chan , and Marjan van der Woude \* .  
S8 Department of Microbiology , University of Pennsylvania , Philadelphia , Pennsylvania 19104 .  
S9 Received 1 March 2002 / Accepted 10 March 2002 .  
S10 ABSTRACT .  
S11 Phase variation of the outer membrane protein Ag43 in E . coli requires deoxyadenosine methylase ( Dam ) and OxyR .  
S12 Previously , it was shown that OxyR is required for repression of the Ag43 - encoding gene , agn43 , and that Dam - dependent methylation of three GATC target sequences in the regulatory region abrogates OxyR binding .  
S13 Here we report further characterization of agn43 transcription and its regulation .  
S14 Transcription was initiated from a sigma 70 - dependent promoter at the G residue of the upstream GATC sequence .

**Annotation**

**Concepts**

Refresh Selected Unselected Focus Export

i	Concept	Name	Score	Freq	Type
<input checked="" type="checkbox"/>	ECK120011302	OxyR	100.00	131	TF
<input checked="" type="checkbox"/>	ECK120009244	oxyR	100.00	131	TU
<input checked="" type="checkbox"/>	ECK120000674	mor	100.00	131	GENE
<input type="checkbox"/>	ECK120003666	yzzX	100.00	75	GENE
<input type="checkbox"/>	ECK120000198	b3387	100.00	73	GENE
<input type="checkbox"/>	ECK120002276	b2092	100.00	60	GENE
<input type="checkbox"/>	ECK120000520	b0344	100.00	27	GENE
<input type="checkbox"/>	COND198	mutation	100.00	16	GC-COLOMB...
<input type="checkbox"/>	EFFECT043	repression	100.00	15	EFFECT
<input type="checkbox"/>	ECK120003891	yfgK	100.00	7	GENE
<input type="checkbox"/>	ECK120009316	speC	100.00	7	TU
<input type="checkbox"/>	ECK120000950	b2965	100.00	7	GENE
<input type="checkbox"/>	COND231	plasmid	100.00	7	GC-COLOMB...
<input type="checkbox"/>	COND050	oxidative...	100.00	6	GC
<input type="checkbox"/>	COND047	nucleotides	100.00	6	GC

**Document PMID 12029051**

Show Pubmed Entry

S6 Dam - and OxyR - Dependent Phase Variation of agn43 : Essential Elements and Evidence for a New Role of DNA Methylation .  
S11 Phase variation of the outer membrane protein Ag43 in E . coli requires deoxyadenosine methylase ( Dam ) and OxyR .  
S12 Previously , it was shown that OxyR is required for repression of the Ag43 - encoding gene , agn43 , and that Dam - dependent methylation of three GATC target sequences in the regulatory region abrogates OxyR binding .  
S17 Since methylation also abrogates OxyR binding , this indicates that methylation plays a dual role in facilitating agn43 transcription .  
S18 In vitro transcription from an unmethylated template was repressed by OxyR ( C199S ) , which resembles the reduced form of OxyR .  
S19 Consistent with this and the role of Dam in OxyR binding , OxyR ( C199S ) protected from DNase I digestion the agn43 regulatory region from 16 to 42 , which includes the three GATC sequences .  
S20 Deletion analyses of the regulatory region showed that a 101 - nucleotide region of the agn43 regulatory region containing the promoter and this OxyR binding region was sufficient for Dam - and OxyR - dependent phase variation .  
S33 Phase variation of agn43 is regulated at the transcriptional level and requires Dam and the oxidative stress response (protein OxyR) ( 15 , 18 ) .  
S39 The second regulator of Ag43 phase variation is OxyR , which is a DNA binding protein that

**Annotation**

**Concepts**

Refresh Selected Unselected Focus Export

i	Concept	Name	Score	Freq	Type
<input checked="" type="checkbox"/>	ECK120011302	OxyR	100.00	131	TF
<input checked="" type="checkbox"/>	ECK120009244	oxyR	100.00	131	TU
<input checked="" type="checkbox"/>	ECK120000674	mor	100.00	131	GENE
<input type="checkbox"/>	ECK120003666	yzzX	100.00	75	GENE
<input type="checkbox"/>	ECK120000198	b3387	100.00	73	GENE
<input type="checkbox"/>	ECK120002276	b2092	100.00	60	GENE
<input type="checkbox"/>	ECK120000520	b0344	100.00	27	GENE
<input type="checkbox"/>	COND198	mutation	100.00	16	GC-COLOMB...
<input type="checkbox"/>	EFFECT043	repression	100.00	15	EFFECT
<input type="checkbox"/>	ECK120003891	yfgK	100.00	7	GENE
<input type="checkbox"/>	ECK120009316	speC	100.00	7	TU
<input type="checkbox"/>	ECK120000950	b2965	100.00	7	GENE
<input type="checkbox"/>	COND231	plasmid	100.00	7	GC-COLOMB...
<input type="checkbox"/>	COND050	oxidative...	100.00	6	GC
<input type="checkbox"/>	COND047	nucleotides	100.00	6	GC

Note: the visualization of selected concepts in the *Document* panel has now been changed from a frame to background highlight.

Document PMID 12908668

Show Pubmed Entry

S1 JOURNAL OF BACTERIOLOGY , Nov . 2011 , p .

S2 5887 - 5897 Vol .

S3 193 , No . 21 0021 - 9193 / 11 / \$ 12.00 doi : 10.1128 / JB . 05872 - 11 Copyright © 2011 , American Society for Microbiology .

S4 All Rights Reserved .

S5 The Escherichia coli MntR Miniregulon Includes Genes Encoding a Small Protein and an Efflux Pump Required for Manganese Homeostasis Lauren S .

S6 Waters, Melissa Sandoval , and Gisela Storz \* Cell Biology and Metabolism Program , Eunice Kennedy Shriver National Institute of Child Health and Human Development , Bethesda , Maryland Received 26 July 2011 / Accepted 28 August 2011 Manganese is a critical micronutrient for cells , serving as an enzyme cofactor and protecting against oxidative stress .

S7 Yet , manganese is toxic in excess and little is known about its distribution in cells .

S8 Bacteria control intracellular manganese levels by the transcription regulator MntR .

S9 When this work began , the only Escherichia coli K - 12 gene known to respond to manganese via MntR repression was mntH

Annotation

Concepts

Refresh Selected Unselected Focus Export Help

i	Concept	Name	Score	Freq	Type	Zone
+	CONDNOUN002	mRNA	100.00	1	COND	Sort Ascending
+	EFFECT043	repression	100.00	26	EFFECT	Sort Descending
+	EFFECT040	repressed	100.00	14	EFFECT	Columns
+	EFFECT036	regulated	100.00	16	EFFECT	Filters
+	EFFECT013	elevated				
+	EFFECT041	repress				
+	EFFECT002	activate				
+	EFFECT037	regulate				
+	EFFECT052	upregul...				
+	EFFECT028	induce				
+	EFFECT027	induced				
+	EFFECT030	induction				
+	EFFECT010	decrease				
+	EFFECT009	decreased				
+	EFFECT055	upregul...				
+	EFFECT033	inhibition	100.00	2	EFFECT	

In order to remove all of the above filters, press the *Refresh* button (it might be necessary to do it twice).

- “AND” Filters: in the *view* menu, you can select filters which are applied in combination, increasingly restricting the number of sentences that are displayed. When you select a type, only sentences containing that type are displayed. If several types are selected, only sentences which contain all selected types are displayed. For example, you are able to inspect only those sentences which contain both genes and effects.

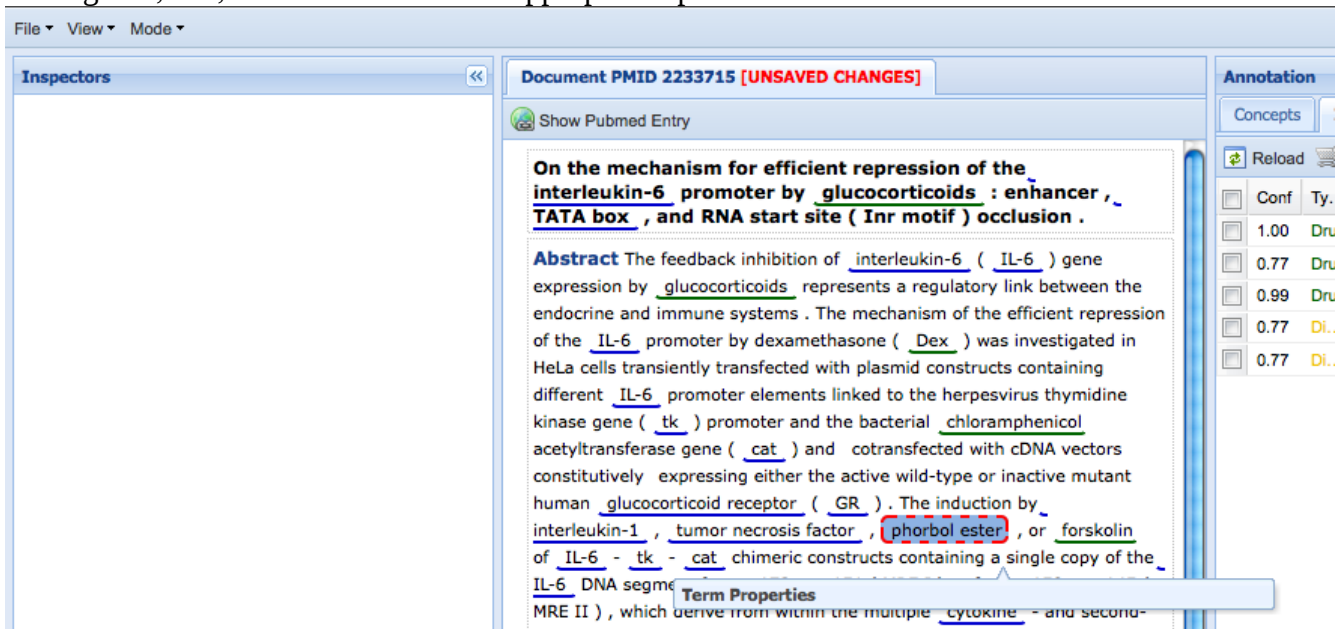
The screenshot shows a software interface with a 'View' menu on the left and a 'Concepts' table on the right. The 'View' menu is open, showing a list of filters under the 'AND' filters section. The filters are: Contains GENE (checked), Contains EFFECT (checked), Contains COND-NOUN (unchecked), Contains GC (unchecked), Contains RNA (unchecked), Contains TF (unchecked), Contains TU (unchecked), and Contains GC-COLOMBOS (unchecked). A 'Remove filter' button is at the bottom of the list. The 'Concepts' table on the right has columns: Concept, Name, Score, Freq, Type, and Zone. It lists various effects like repression, repressed, regulated, elevated, repress, activate, regulate, upregul..., induce, induced, induction, decrease, decreased, upregul..., inhibition, and represses.

Concept	Name	Score	Freq	Type	Zone
EFFECT043	repression	100.00	26	EFFECT	text
EFFECT040	repressed	100.00	14	EFFECT	text
EFFECT036	regulated	100.00	16	EFFECT	text
EFFECT013	elevated	100.00	6	EFFECT	text
EFFECT041	repress	100.00	8	EFFECT	text
EFFECT002	activate	100.00	1	EFFECT	text
EFFECT037	regulate	100.00	6	EFFECT	text
EFFECT052	upregul...	100.00	6	EFFECT	text
EFFECT028	induce	100.00	1	EFFECT	text
EFFECT027	induced	100.00	7	EFFECT	text
EFFECT030	induction	100.00	5	EFFECT	text
EFFECT010	decrease	100.00	1	EFFECT	text
EFFECT009	decreased	100.00	2	EFFECT	text
EFFECT055	upregul...	100.00	2	EFFECT	text
EFFECT033	inhibition	100.00	2	EFFECT	text
EFFECT042	represses	100.00	1	EFFECT	text

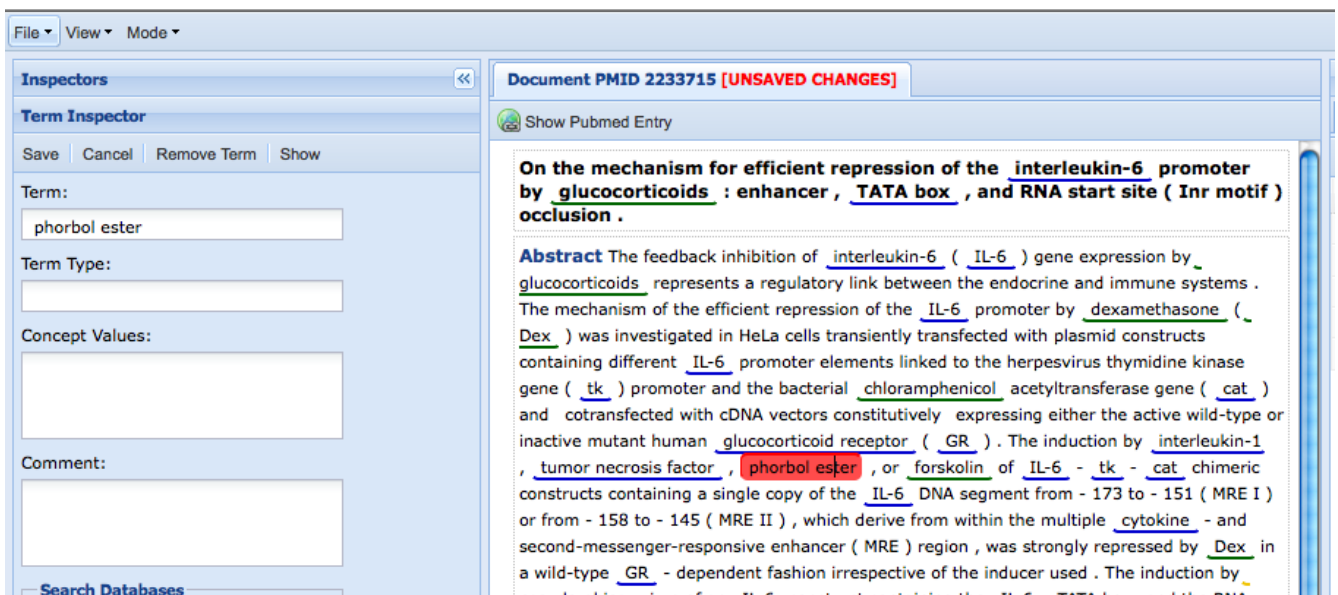
Note that unchecking the boxes does not work correctly. Instead you need to select *Remove filter* to get back to the original situation.

## 5. The Term Inspector

You can manually add terms which were not correctly annotated as follows. Double-click on a word to be able to annotate it in the inspector. The first click selects the word (a red dotted frame appears), the second click opens the term inspector (the word is highlighted in red and the *Inspectors* panel becomes visible on the left side). If you want to create a multi-term word, single-click on one of the words, then its neighbour, etc., until the term has the appropriate span.



Then, when you click again, the term inspector opens and the span of words is highlighted in red.



If you have made an erroneous selection, click on *Remove Term* in the *Inspector* panel. You can also remove terms by clicking them in the *Document* panel while pressing the SHIFT key.

In the *Term Inspector*, you can manually edit the concept and the type of a term, leave a comment or browse term databases (click the down arrow next to *Search Databases*). The specific set of DBs available depends on the version of ODIN, but typically include Entrez, Uniprot and a reference database for the specific application. The following screenshots give a browsing example. First, an example from CTD. Click on a term in the document panel ('pseudorabies', in red in the example below). Tick *CTD* in the *Inspectors* panel (left), then click *Search Terms*. As this term is ambiguous, we are given a selection. We choose 'Diseases'.

The image displays three screenshots from the CTD (Comparative Toxicogenomics Database) interface. The leftmost screenshot shows the 'Term Inspector' panel with 'pseudorabies' as the term and 'disease' as the type. The middle screenshot shows the 'Keyword Query Results' for 'pseudorabies', listing 5 items: Chemicals (1), Diseases (1), Genes (2), GO Terms (0), and Organisms (0). The rightmost screenshot shows the 'Pseudorabies' detail page, including synonyms (Aujeszky Disease), definition (A highly contagious herpesvirus infection), categories (Animal disease, Nervous system disease, Viral disease), and MeSH ID (D011557).

Notice that this function will not work if your browser has a popup blocker (as it is the default in Chrome). In order to use it, deactivate the popup blocker.

Second, an example from 'PharmGKB' on 'dexamethasone'.

The screenshot shows the PharmGKB website interface. At the top, there's a navigation bar with links: HOME | PUBLICATIONS | FEEDBACK | SIGN IN | and a search bar. Below this is a secondary navigation bar with links: Home | Search | Download | Help | Consortia. The main content area is titled 'Search for' and shows the search term 'dexamethasone'. Below the search bar, there's a 'Database Search' section with a 'view legend' link. A 'Limit results to:' section allows filtering by Genes, Variants, Drugs, Diseases, Pathways, Publications, Dosing Guidelines, Drug Labels, Clinical Annotations, and Genetic Tests. The results are sorted by relevance, showing 'Results 1 - 20 of 401'. The first result is for 'Drug: dexamethasone [ pgx research ]', listing alternate names like Adexone, Aeroseb-D, and Anaflogistico. The second result is for 'Gene: RASD1', listing alternate names like RAS, dexamethasone-induced 1, and AGS1. The third result is for 'Drug: thiabendazole', listing alternate names like Apl-Luster, Arbotecl, and Bioguard. The fourth result is for 'Drug: ciprofloxacin'.

Within the PharmGKB database, with two additional clicks you might get to the screen shown below, depending on what you are looking for.

The screenshot shows the PharmGKB website interface for the drug 'dexamethasone'. The browser address bar shows the URL: pharmgkb.org/drug/PA449247?previousQuery=dexamethasone#1. The page title is 'dexamethasone [PharmGKB]'. The navigation bar includes links: HOME | PUBLICATIONS | FEEDBACK | SIGN IN | and a search bar. Below this is a secondary navigation bar with links: Home | Search | Download | Help | Consortia. The main content area is titled 'DRUG/SMALL MOLECULE: dexamethasone' and includes a 'from search: dexamethasone, dexamethasone' link. Below this is a tabbed interface with tabs: Clinical PGx, PGx Research, Overview, Properties, Pathways, Is Related To, Publications, and Downloads/LinkOuts. The 'Overview' tab is selected. The 'Overview' section displays three columns of information: 'Generic Names' (DEX, DXM, Desametasone, Desametasone [Dcit], Desamethasone, Dexametasona [INN-Spanish], Dexamethasone Acetate), 'Trade Names' (Adexone, Aeroseb-D, Aeroseb-Dex, Anaflogistico, Aphtasolon, Aphthasolone, Auxiron), and 'Brand Mixture Names' (Ak Trol Suspension, (Dexamethasone + Neomycin Sulfate + Polymyxin B Sulfate), Ciprodex (Ciprofloxacin), (Ciprofloxacin Hydrochloride) + Dexamethasone, Cresonphene Liq (Camphor +). To the right of the text is a chemical structure diagram of dexamethasone.

## Repeated Term Mode

The *Term Inspector* has two modes of operation, which can be selected in the *Mode* menu: *Single Term* and *Repeated Term*. In *Single Term* mode, only the single instance which you select is changed. In *Repeated Term* mode, all occurrences inside the document are changed. In order to assist the annotator in his or her decision whether all occurrences are of the same type, ODIN only displays the sentences containing the term that is being edited.

Notice that *Repeated Term* mode can be applied only to existing terms. It cannot be applied to words which have not already been marked as terms (if you do it, the entire document seems to disappear. In this case, just unselect *Repeated Term* mode to go back to normal).

While the core of ODIN is similar in all versions, it is a flexible tool and the version that is adapted to your task may look different.

We will look at two typical tasks in the following chapters: working with interactions in section 6, and with organisms in section 7.

## 6. Working with Interactions

We are now going to look at the **interactions** that were suggested by the system. Select one of the interactions: the terms in the document which participate in this interaction will be highlighted and a colored frame will be placed around them to allow easy identification.

In the following screenshot, the relation between “Pulmonary edema” and “TNF-alpha” has been selected. Note that a search has been performed in the reference database to confirm that the gene “TNF” actually corresponds to “TNF-alpha”.

The screenshot displays the OntoGene.org web application. The main window shows a document titled "Document PMID 8318674 [UNSAVED CHANGES]". The abstract text is visible, with terms like "Pulmonary edema" and "TNF" highlighted. An inset window shows the "TNF" entry in the Comparative Toxicogenomics Database (CTD), listing synonyms and top interacting chemicals. On the right, the "Interactions" panel is active, showing a table of interactions between concepts and genes.

Con...	Type 1	Name 1	Type 2	Name 2				
<input type="checkbox"/>	1.00	disease	Pulmonary Edema	gene	KIAA0101	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	1.00	disease	Pulmonary Edema	gene	TNFB	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	1.00	disease	Pulmonary Edema	gene	TNF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	1.00	disease	Pulmonary Edema	gene	ATMS	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	1.00	disease	Pulmonary Edema	gene	PAF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.95	gene	TNFB	gene	KIAA0101	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.95	gene	TNF	gene	KIAA0101	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.95	gene	ATMS	gene	TNFB	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.95	gene	ATMS	gene	TNF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.95	gene	PAF	gene	TNFB	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.95	gene	PAF	gene	TNF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.86	disease	Pulmonary Edema	gene	LITAF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.86	disease	Pulmonary Edema	gene	TNF-ALPHA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.86	disease	Pulmonary Edema	gene	TNFA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	LITAF	gene	KIAA0101	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	TNF-ALPHA	gene	KIAA0101	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	TNF-ALPHA	gene	ATMS	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	TNF-ALPHA	gene	PAF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	ATMS	gene	LITAF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	TNFA	gene	KIAA0101	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	TNFA	gene	ATMS	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	PAF	gene	LITAF	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	0.82	gene	PAF	gene	TNFA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

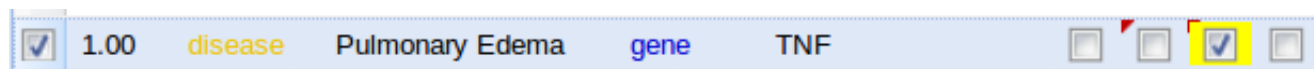
The user can then decide if the interaction is correct or not by clicking one of the options to the right of the *Interactions* panel.

If the interaction is believed to be correct, the first box should be ticked (see picture on the right).

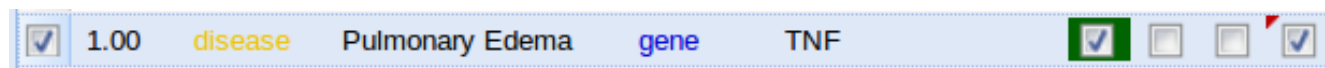
If it is believed to be wrong, the second box should be ticked.

This close-up view of the "Interactions" panel shows the same table as the previous screenshot. The row for the interaction between "Pulmonary Edema" (disease) and "TNF" (gene) is selected. The first checkbox in the rightmost column is checked, indicating that the interaction is correct. The second checkbox is also visible, representing the option to mark the interaction as incorrect.

There are two other options. In case the abstract does not provide sufficient information and the user is not able to make a decision without consulting the full text of the paper, the third box should be ticked, as in the picture below:



Finally, if the document actually expresses that there is NO interaction between the two entities (i.e. it is expressing a negative interaction), the user should tick the last box (which automatically select also the first one).



You can optionally resize the columns of the interaction table, and remove some of them. If you hover over the column titles, a down-arrow between the columns will appear: use it in order to open a menu. The menu contains options for sorting, and a submenu called *Columns*, which can be used to select which columns to show. For example, the columns *Concept1* and *Concept2* could be removed because the same information can be obtained by hovering the mouse over the columns *Name1* and *Name2*. An additional submenu (called *Filters*) might appear in some columns. Its function has been explained in section 4.

The screenshot shows the OntoGene.org web application in a Mozilla Firefox browser. The main content area displays a document entry for PMID 2233715, titled "On the mechanism for efficient repression of the Interleukin-6 promoter by glucocorticoids: enhancer, TATA box, and RNA start site (lrr motif) occlusion". The abstract text is visible, discussing the feedback inhibition of IL-6 gene expression by glucocorticoids. On the right side, there is an "Annotation" panel with a tab for "Interactions". Below this tab is a table with columns: Conf, Type 1, Name 1, Type 2, Name 2, and a set of checkboxes. The table contains two rows of data. A context menu is open over the "Name 1" column header, showing options for "Type 1", "Name 1", "Type 2", "Concept 2", and "Name 2". The "Columns" submenu is also visible, showing checkboxes for "Type 1", "Concept 1", "Name 1", "Type 2", "Concept 2", and "Name 2".

A double click on the specific name or concept column opens a separate browser window where you can inspect the corresponding concept from the source database (which depends on the specific ODIN customization, it's CTD in the example below). This functions works also in the *Concepts* panel in a similar way. Notice that if you have a popup blocker this function will not work correctly.

efficient repression of the interleukin-6 promoter by glucocorticoids : enhancer , TATA box motif ) occlusion .

tion of interleukin-6 ( IL-6 ) gene expression by glucocorticoids represents a regulatory link between stems . The mechanism of the efficient repression of the IL-6 promoter by dexamethasone ( Dex )

Annotation

Concepts Interactions

Reload Export

Co...	Type 1	Concept 1	Name 1	Type 2	Co
3.30	chem	MESH_D005576	Forskolin	gene	18:
3.30	chem	MESH_D042755	Tetradecanoylp...	gene	18:
			Cyclic AMP	gene	18:
			Glucocorticoids	gene	18:
			OFA	gene	69:
			OFA	gene	84:
			OFA	gene	41:
			OFA	gene	25:
			OFA	gene	35:
			Dexamethasone	gene	18:
			ACETYLTRANS...	gene	18:
			Chloramphenicol	gene	18:
			Pseudorabies	gene	18:
			GR	gene	18:
			phorbol	gene	18:
			OFA	gene	21:
			OFA	gene	41:
			OFA	gene	38:
			OFA	gene	70:
			OFA	gene	37:
			DNASE1	gene	18:
			Tumor Necrosis...	gene	18:
			OFA	gene	37:
			Thymidine	gene	18:
			Interleukin-1alpha	gene	18:
			Neoplasms	gene	18:
			OFA	gene	80:
			TNF-ALPHA	gene	18:
			Dexamethasone	gene	35:
			Forskolin	gene	35:

ctdbase.org/detail.go?type=chem&acc=D005576

Reader

Bonjour ICEqueries ICE online ICE Online ANS ES CL DG GMail CoNNL-DG mOG ACE

Forskolin | CTD

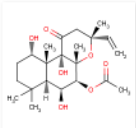
ctd Illuminating how chemicals affect human health.

Comparative Toxicogenomics Database

Home Search Analyze Download Help

Forskolin

Basics Gene Interactions Genes Diseases Comps Pathways GO References

Name	Forskolin
CAS Type 1 Name	1H-Naphtho(2,1-b)pyran-1-one, 5-(acetyloxy)-3-ethenyldecahydro-6,10,10b-trihydroxy-3,4a,7,7,10a-pentamethyl-
Equivalent Term	Coleonol
CAS Registry Number	66428-89-5
Definition	Potent activator of the adenylate cyclase system and the biosynthesis of cyclic AMP. From the plant Coleus forskohlii. Has antihypertensive, positive inotropic, platelet aggregation inhibitory, and smooth muscle relaxant activities; also lowers intraocular pressure and promotes release of hormones from the pituitary gland.
Structure	
Top Interacting Genes	CFTR CYP19A1

## 7. Constraining Organisms

In the following example, we show a version of ODIN that works with information on organisms. Depending on your customization and field of application, this may not be available.

We open the sample PubMed file 1226314, and select organism and term tables from the *View* menu, if your version of ODIN offers them. Your screen may now look as follows.

The screenshot displays the OntoGene.org web application interface. The main window is titled "Document PMC 1226314" and contains the abstract and introduction of a PubMed article. The abstract discusses the role of Gfi-1B in erythropoiesis and its regulation by GATA-1. The introduction provides background on Gfi-1B and its function in erythroid lineage cells.

On the right side, the "Annotation" panel is visible, showing a table of terms and their associated concepts. The table has columns for #, Term, Concepts %, Typ., and A. The terms listed include GATA-1, Gfi-1B, myb, and RPMI, with their corresponding concepts and types.

#	Term	Concepts %	Typ.	A.
1	GATA-1	821990_ARATH 1...	GEN	4
2	Gfi-1B	14582_MOUSE 8...	GEN	2
3	GATA	1232960_RHIME ...	GEN	2
4	Gfi-1B	14582_MOUSE 8...	GEN	2
5	GATA-1	821990_ARATH 1...	GEN	4
6	GATA-1	821990_ARATH 1...	GEN	4
7	Gfi-1B	14582_MOUSE 8...	GEN	2
8	Gfi-1B	14582_MOUSE 8...	GEN	2
9	GATA-1	821990_ARATH 1...	GEN	4
10	myb	4602_HUMAN 32...	GEN	3
11	MEL	4218_HUMAN 17...	GEN	2
12	Gfi-1B	14582_MOUSE 8...	GEN	2
13	myb	4602_HUMAN 32...	GEN	3
14	GATA-1	821990_ARATH 1...	GEN	4
15	Gfi-1B	14582_MOUSE 8...	GEN	2
16	myb	4602_HUMAN 32...	GEN	3
17	Gfi-1B	14582_MOUSE 8...	GEN	2
18	GATA-1	821990_ARATH 1...	GEN	4
19	DNA bind...	REMO_ARATH	PROT	1
20	GATA-1	821990_ARATH 1...	GEN	4
21	Gfi-1B	14582_MOUSE 8...	GEN	2
22	Gfi-1B	14582_MOUSE 8...	GEN	2
23	GATA-1	821990_ARATH 1...	GEN	4
24	RPMI	1231917_RHIME	GEN	1

The article deals with human genes and proteins. If we click the *Organism* tab of the *Annotation* panel we see that indeed the system assign the highest probability (51.3%) to human.

We can discard all non-human concepts (e.g. interpretations terms as non-human proteins) as follows: tick all organisms except human, then click on the – *selected* symbol, as shown below.

The screenshot shows the OntoGene.org web application. The main window displays a document titled "Document PMC 1226314". The document content includes an abstract and an introduction section, both discussing the Gfi-1B gene and its role in erythropoiesis. The abstract states: "GATA-1 mediates auto-regulation of Gfi-1B transcription in K562 cells". The introduction states: "Gfi-1B ( growth factor independence - 1B ) is an erythroid-specific Gfi - family transcriptional factor , which was identified by low stringency hybridization screening with a partial Gfi-1 cDNA probe ( 1 ) . Both Gfi-1 and Gfi-1B contain a SNAG domain that mediates transcriptional repression and a zinc finger domain at its C - terminus for their DNA binding to the TAAATCAC ( A/T ) GCA recognition sequence ( 1 - 3 ) . Expression of Gfi-1B is confined in erythroid lineage cells and megakaryocytes in human ( 4,5 ) , whereas Gfi-1 is more abundant in the lymphopoietic thymus ( 6 - 8 ) . So far , p21 ( cip1 / waf1 ) , Socs1 and Socs3 are known as the target genes of Gfi-1B - mediated transcriptional repression ( 1,9 ) . Since p21 is a cell cycle inhibitor and SOCS family members are known to suppress cytokine signaling , the functional role of Gfi-1B is considered to be important in controlling proliferation of erythrocyte/megakaryocyte-lineage cells . Its importance in erythropoiesis has been further highlighted by gene targeting experiment showing that Gfi-1B gene disruption results in embryonic lethality due to loss of red blood cell formation ( 10 ) . Enforced expression experiment in early erythroid progenitor cells has shown that Gfi-1B induces a drastic expansion of erythroblast independent of its SNAG repression domain with a parallel".

On the right side, there is an "Annotation" panel. It has tabs for "Organisms" and "Terms". The "Organisms" tab is active, showing a list of organisms with checkboxes and numerical values. The list includes: MOUSE, DROME, BPP4, CERAE, ARATH, NEUCR, PIG, RAT, BPT4, and STRPU. All checkboxes are checked. A "Refresh" button and a "Selected" button are also present. A tooltip is visible over the "Selected" button, stating: "Remove all protein/genes concepts in terms referring to the selected organism(s). Allows to quickly reduce all false positives genes/proteins that arise from a wrong organism."

At the bottom of the page, there is a footer with the text: "Documentation as PDF :: Contact: [odin@ontogene.org](mailto:odin@ontogene.org) :: For project information visit [www.ontogene.org](http://www.ontogene.org)".

All organisms except for human disappear. Also in the text, fewer terms are highlighted. If we click the *Terms* tab no change is immediately apparent, we first need to press the *Refresh* button to see only human terms. If we click on a term in the text, the term inspector only gives human concept values, which considerably reduces ambiguity.

## 8. Saving your work

In the *File* menu, you can save your annotations. Note that the save option might not be available in demo versions. If you save a modified article, a new file will be created and named in the format PMID-CID.xml (Pubmed-id and curator identifier). If you reload the article using the same curator id, the system will use this file, if available. This means your selections up to that point will be there when reloading an article that has been modified and saved before.

2233715 [UNSAVED CHANGES]

Entry

mechanism for efficient repression of the **interleukin-6** promoter by **glucocorticoids** : **TATA box** , and **RNA start site ( Inr motif ) occlusion** .

Feedback inhibition of **interleukin-6** ( **IL-6** ) gene expression by **glucocorticoids** represents a regulatory the endocrine and immune systems . The mechanism of the efficient repression of the **IL-6** promoter by **ne** ( **Dex** ) was investigated in HeLa cells transiently transfected with plasmid constructs containing **IL-6** promoter elements linked to the herpesvirus thymidine kinase gene ( **tk** ) promoter and the bacterial chloramphenicol acetyltransferase gene ( **cat** ) and cotransfected with cDNA vectors constitutively expressing either the active wild-type or inactive mutant human glucocorticoid receptor ( **GR** ) . The induction by interleukin-1 , tumor necrosis factor , phorbol ester , or forskolin of **IL-6** - **tk** - **cat** chimeric constructs containing a single copy of the **IL-6** DNA segment from - 173 to - 151 ( MRE I ) or from - 158 to - 145 ( MRE II ) , which derive from within the multiple cytokine - and second-messenger-responsive enhancer ( MRE ) region , was strongly repressed by **Dex** in a wild-type **GR** - dependent fashion irrespective of the inducer used . The induction by pseudorabies virus of an **IL-6** construct containing the **IL-6** TATA box and the RNA start site ( " initiator " or **Inr** element ) but not the MRE region was also repressed by **Dex** in the presence of wild-type **GR** . DNase I footprinting showed that the purified DNA-binding fragment of **GR** bound across the MRE , the TATA box , and the **Inr** site in the **IL-6** promoter ; this footprint overlapped that produced by proteins present in nuclear extracts from uninduced or induced HeLa cells . Imperfect palindromic nucleotide sequence motifs moderately related to the consensus **GR** - responsive element ( **GRE** ) motif were present at the **Inr** , the TATA box , and the MRE II site in the **IL-6** promoter ; although MRE I and a **GR** - binding site between - 201 and - 210 in **IL-6** both lacked a discernible inverted repeat motif , their sequences showed considerable similarity with negative **GRE** sequences in other **Dex** - repressed genes . Surprisingly , chimeric genes containing MRE II , which lacks a recognizable GACGTCA cyclic AMP - and phorbol ester-responsive motif , were strongly induced by both phorbol ester and forskolin , suggesting that MRE II ( ACATTGCACAATCT ) may be the prototype of a novel cyclic AMP - and phorbol ester-responsive element . Taken together , these observations suggest that ligand-activated **GR** represses the **IL-6** gene by occlusion not only of the inducible **IL-6** MRE enhancer region but also of the basal **IL-6** promoter elements .

Interleukin-1 ; **Interleukin-6** ; Oligonucleotide Probes ; RNA , Neoplasm ; Receptors , Glucocorticoid ; Tumor Necrosis Factor-alpha ; Tetradecanoylphorbol Acetate ; **Dexamethasone** ; Forskolin ; Base Sequence ; **Dexamethasone** ; pharmacology ; Enhancer Elements , Genetic ; drug effects ; Feedback ; Forskolin ; pharmacology ; Gene Expression ; drug effects ; Genes , Suppressor ; drug effects ; HeLa Cells ; drug effects ; immunology ; Humans ; Interleukin-1 ; pharmacology ; **Interleukin-6** ; genetics ; Molecular Sequence Data ; Oligonucleotide Probes ; Promoter Regions , Genetic ; RNA , Neoplasm ; drug effects ; genetics ; Receptors , Glucocorticoid ; genetics ; metabolism ; Restriction Mapping ; Second Messenger Systems ; TATA Box ; drug effects ; Tetradecanoylphorbol Acetate ; pharmacology ; Transcription , Genetic ; Transfection ; Tumor Necrosis Factor-alpha ; pharmacology ;

Annotation

Concepts Interactions

Reload Finish & Save Help

Conf	Type 1	Name 1	Type 2	Name 2				
<input checked="" type="checkbox"/>	0.99	Drug	dexamethasone	Gene	IL6	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	1.00	Drug	glucocorticoids	Gene	IL6	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

http://kitt.cl.uzh.ch/kitt/bcms/pharmgkbmeB/# | project information visit [www.ontogene.org](http://www.ontogene.org) :: Logged in as:

## 9. Summary of database search options

Inside ODIN it is possible to launch searches into reference databases in several ways. Here you can find a brief summary of the available options.

1. From the *Inspector* panel: when editing a term, you can use the button '*Search Term Text*'.
2. From the *Concepts* tab in the *Annotation* panel: when clicking on the concept name or id, a search in the reference DB (which depends on the application) can be launched.
3. From the *Interactions* tab in the *Annotation* panel: clicking on the name of one of two entities participating in the interaction launches a search in the reference DB. This function is not always available, depending on the application.

## 10. Known Bugs

- cdt version: Terms in term tab in the annotation panel do not change to the new file if one file is closed with unsaved changes and a new file is opened
- ctd version: If there are subordinate titles in the abstract (such as Background or Methods), all of these are converted to “Abstract”.
- ctd version: Tabs in the Annotation panel are not parallel anymore if they are added again.
- ccg version: File → Reload does not work once some changes have been made. Then it is also not possible to load a new file.